

REMARKS

Claims 1-14, 29-31, 33-39, 45-49 and 53 were pending in the present application. Claims 1 and 45 are amended herein, support for which can be found throughout the specification and original claims, for example, at page 20, the first and the last paragraphs, at page 21, the last full paragraph, and at page 22, the last two paragraphs of the specification (for instance, the alkyl, alkenyl, heteroaryl, and cycloheteroalkyl in R₅ are optionally substituted). No new matter has been added. Upon entry of the present amendment, claims 1-14, 29-31, 33-39, 45-48, and 53 will remain pending.

As a preliminary matter, Applicants acknowledge with gratitude the courtesies extended to their representative, Feng Shao, during a telephonic interview with Examiner Covington on July 02, 2008.

I. Telephone Interview

During the telephonic interview with Examiner Covington on July 02, 2008, the scope of the rejections in the Office Action, including clarification of the rejections, was discussed. During the interview, Examiner Covington agreed the Office Action should be revised to:

1. Claims 3-11 remain allowable, as indicated in the previous Office Action mailed on November 27, 2007. Accordingly, the rejections in this Office Action under 35 U.S.C. § 112, first paragraph do not apply to claims 3-11.
2. The rejections in this Office Action under 35 U.S.C. § 112, first paragraph are directed to the scope of “heteroaryl” and “cycloheteroalkyl,” in the definition of R⁴. (including those of R⁵ and R⁶.)

Moreover, during the interview, Examiner Covington asked that Applicants, through their representative, to rewrite the definitions of R⁴, R⁵ and R⁶ to obviate any recursive problems.

II. Rejections under 35 U.S.C. § 112, first paragraph

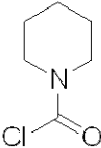
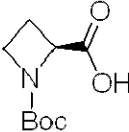
Claims 1, 2, 12-14, 29-31, 33-39, 45-48, and 53 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to meet the enablement requirement. Despite acknowledging that compounds of formula IX where R₄ may contain a piperidine, pyrrole, pyridine, thiophene, or dioxane are enabled, the Action alleges that the specification "provides no guidance as to what other rings might be suitable and there is no basis in the prior art directed to similar compounds having the same activity as herein." See Action at page 2. The Action also alleges that "there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will share the same physiological properties since they are so structurally dissimilar"; and alleges that the compounds embraced by the claims would not be produced by the same process. *Id.* at page 3. Applicants respectfully request reconsideration in light of amended claims 1 and 45.

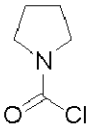
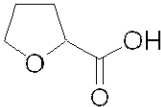
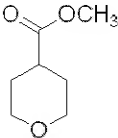
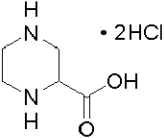
At the outset, Applicants respectfully point out that the definition of R₄ refers to "hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)_nR₅, -CONR₅R₆, or SO₂R₅," wherein said aryl, aralkyl, alkyl, or cycloalkyl can be optionally substituted (i.e., **R₄ does not include heteroaryl or cycloheteroalkyl directly**). Nevertheless, although Applicants believe that claims 1 and 45, in the original or previously presented form, are enabled, solely to expedite prosecution and without disclaimer of subject matter, claims 1 and 45 have been amended herein. More specifically, **the 4-8 membered heteroaryl and the 5-10 membered cycloheteroalkyl rings in R⁵ and R⁶ (and in NR₅R₆) are amended to recite specific heteroaryl and cycloheteroalkyl radicals**. Applicants respectfully assert that those skilled in the art can readily make and use each of the claimed process/products in view of the teaching of the specification.

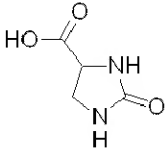
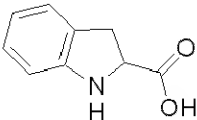
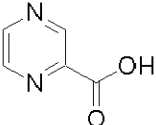
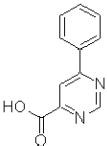
Those skilled in the art can readily select starting materials to make and use the claimed processes in view of the teaching of the specification. For example, in step 4 of Scheme I (page 24 of the specification), compound 5 (a cyclic, secondary amine) can be reacted with R₄L wherein L is a leaving group such as halogen. Those skilled in the art can recognize such a coupling reaction (acid halide + amine → amide). Those skilled in the art can also recognize that an acid can be converted to its corresponding acid chloride and then

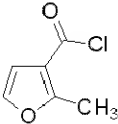
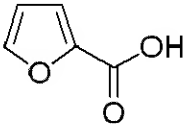
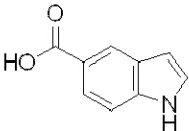
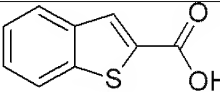
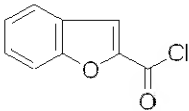
the acid chloride can be used to make the amide. Alternatively, an acid (instead of an acid halide), in the presence of an amide coupling reagent, can also be used for making the same amide. Accordingly, those skilled in the art can readily choose acids or acid halides which contain heteroaryl or cycloheteroalkyl in such coupling reaction (especially the specific heteroaryl and cycloheteroalkyl radicals recited in the amended claims). Some exemplary compounds of R_4L^1 (wherein R_4 is $-C(O)_nR_5$ or $-CONR_5R_6$; and wherein R_5 or NR_5R_6 contains optionally substituted heteroaryl or cycloheteroalkyl; and L^1 is halogen or OH), which are readily available from a commercial catalog such as Sigma-Aldrich catalog, are listed in the Table below.

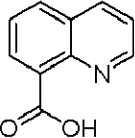
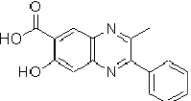
Table 1. Exemplary available starting materials

Compound Name	CAS #	Structure	Aldrich (Sigma, or Fluka) product number
1-piperidinecarbonyl chloride	CAS #: 13939-69-0		518522
1-(tert-butoxycarbonyl)-2-azetidinecarboxylic acid	CAS #: 51077-14-6		78324
1-pyrrolidinecarbonyl chloride	CAS #: 1192-63-8		206350

			
tetrahydro-2-furancarboxylic acid	CAS #: 16874-33-2		341517
methyl tetrahydro-2H-pyran-4-carboxylate	CAS #: 110238-91-0		40199
2-piperazinecarboxylic acid dihydrochloride	CAS #: 3022-15-9		484903

2-oxo-4-imidazolidinecarboxylic acid	CAS #: 41371-53-3		860166
2-indolinecarboxylic acid	CAS #: 78348-24-0		302244
2-pyrazinecarboxylic acid	CAS #: 98-97-5		P56100
6-phenyl-4-pyrimidinecarboxylic acid	CAS #: 28668-32-8		633674

2-methyl-3-furoyl chloride	CAS #: 5555-00-0		678597
2-furoic acid	CAS #: 88-14-2		F20505
1H-indole-5-carboxylic acid	CAS #: 1670-81-1		I5400
1-benzothiophene-2-carboxylic acid	CAS #: 6314-28-9		467464
1-BENZOFURAN-2-CARBONYL CHLORIDE	CAS #: 41717-2-8-6		R703338

8-quinolinecarboxylic acid	CAS #: 86-59-9		367796
7-HYDROXY-3-METHYL-2-PHENYL-6-QUINOXALINECARBOXYLIC ACID			L101605

Applicants respectfully assert that those skilled in the art can readily recognize the reaction for making amides (or sulfonamides) in the claims. The Office did not carry out its burden when asserting that the compounds in the claims cannot “be produced by the same process.” *See* Office Action at page 3. Moreover, the definition of heteroaryl groups (which R₅ and R₆ may contain) is amended to those shown hereinabove. In addition, Applicants respectfully assert those skilled in the art would not think that heteroaryl would “sterically hinder or prevent the making of the starting materials, intermediates or final products.” *See id.*

The Office’s discussion regarding the definitions of heteroaryl and cycloheteroalkyl on pages 3-4 of the Office Action becomes moot because the definitions on pages 19 and 20 are clear and definite. *See* pages 19 and 20 of the specification [the heteroatoms are selected from N, S and O. Accordingly, they cannot be other elements such as phosphorous, arsenic, selenium or tellurium]. Moreover, substituents (in various R groups) in claims 1 and 45 are amended. Those skilled in the art can readily recognize the scope and meaning of each variable. In view of the examples and schemes given in the application, those skilled in the art would be able to make and use the claimed invention without undue experimentation.

In addition, the specification teaches test procedure for TACE inhibition. *See* Specification at page 75 (providing both test procedure and data for compound Example 18). Those skilled in the art can readily follow the procedure in testing other compounds in the independent claim 45.

In view of the foregoing amendment, Applicants respectfully assert that claims 1, 2, 12-14, 29-31, 33-39, 45-48, and 53 are enabled, and request that the claim rejection be withdrawn.

III. Conclusion

In view of the foregoing, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 981-4142 if there are any questions regarding the present application.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to deposit account 50-0436.

Respectfully submitted,

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